118. *On Sinomeninol*[1)]

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Sinomenine (I) was reduced by $LiAlH_4$. It gave sinomeninol (II), which formed a diacetyl derivative with acetic anhydride and dihydrosinomeninol (III) on catalytic reduction. These two reactions showed that in sinomeninol the original ketone group was reduced to alcohol, but the double bond was left intact.

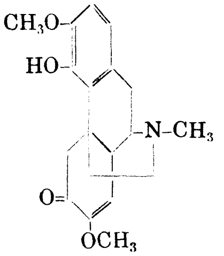
On hydrolysis with 20% hydrochloric acid, sinomeninol gave β-dihydrosinomeninone (IV), which was identical with that obtained by catalytic reduction of sinomeninone (V). As the constitution of β-dihydrosinomeninone obtained in this reaction must be 7-keto-6-ol, if no molecular rearrangement had occurred in the hydrolysis, our former conclusion as to the constitution of α- and β-dihydrosinomeninone[2)], seemed to have become untenable. We formerly concluded that the constitution of the both substances were 6-keto-7-ol and the difference existed only in the diastereoisomerism of alcohol group in 7. Now we think we can conclude safely that α-dihydrosinomeninone is 7-hydroxy-(+)-dihydrothebainone (VI) and β-dihydrosinomeninone is 6-hydroxy-(+)-dihydrothebainone-7 (IV). To this conclusion, we could bring further evidences. Moreover, it may be more reasonable to think that in catalytic reduction of sinomeninone, each of the two ketone groups is reduced equally, though in different proportion, than to assume that the reduction is carried on preferably on 7-ketone group and in diastereoisomeric manner.

By boiling sinomeninol with 55% sulphuric acid, (+)-dihydrocodeinone (VII) was obtained in 30% yield. The same is true of β-dihydrosinomeninone. The formation of (+)-dihydrocodeinone from α-dihydrosinomeninone (VI) and dihydrosinomenine can simply be explained by anionotropy of 7-hydroxyl group over the adjacent ketone group[3)]. But, in this case, the transformation of β-dihydrosinomeninone into α-dihydrosinomeninone must forego to the anionotropy and oxide ring formation. Hitherto, the rearrangement of α-dihydrosinomeninone into β-dihydrosinomeninone was easily realized by heating alone, heating with acid or alkali, but not the vice versa[4)]. We have now treated pure β-dihydrosinomeninone (m.p. 103°) with 22.5% sulphuric acid on water bath and obtained the α-derivative in a small yield.

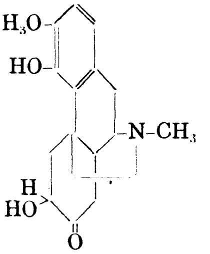
By acetolysis in a sealed tube, both α- and β-dihydrosinomeninone gave the same phenanthrene of m.p. 166°. The melting point was unaltered with admixture of 3-methoxy-4, 6-diacetoxyphenanthrene (m.p. 166°) prepared from sinomeninone[5]. But the yield in both cases was too scanty (0.1%) and we can conclude nothing from this experiment.

On the contrary, the reduction of α- and β-dihydrosinomeninone with Na-amalgam gave a more reliable result. α-Dihydrosinomeninone gave (+)-dihydrothebainone in this treatment, as was reported already[2]. But β-dihydrosinomeninone gave (+)-dihydrothebainone-7,[6] which was reduced catalytically to (+)-dihydrothebainol-7. These two substances coincided well with those obtained from tetrahydrosinomeninone (IX).

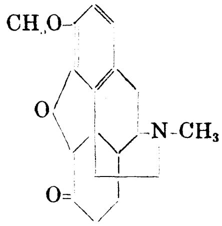
The misjudgement, to which we (K. G. and K. M.) were led formerly, was perhaps caused by the contamination of β-dihydrosinomeninone with α-substance, as in the related experiment, the former substance was prepared from the latter by heating with hydrochloric acid. Moreover, dihydrothebainone-7 was unknown at that time. It was prepared only later by K. M. from tetrahydrosinomeninone[7].



I. Sinomenine
II. Sinomeninol (HOH in 6)
III. Dihydrosinomeninol (No double bond in II)



IV. β-Dihydrosinomeninone
V. Sinomeninone (O in 6)
VI. α-Dihydrosinomeninone (O in 6, HOH in 7)
VIII. (+)-Dihydrothebainone-7 (H_2 in 6)
IX. (+)-Tetrahydrosinomeninone (HOH in 7)



VII. (+)-Dihydrocodeinone

Experimental

Sinomeninol (II)

Well dried sinomenine (6 gr.) was reduced by boiling with $LiAlH_4$ (1.1 gr.) in tetrahydrofurane (100 cc.) for six hours. The excess of $LiAlH_4$ was destroyed by ice water and the base was taken up in chloroform. The chloroform residue was twice recrystallized from acetone. Short prisms. M. p. 214°. Yield 80%. Very soluble in methanol. $[\alpha]_D^{23} = -188.6^\circ$ (c 1.675, chlf.). (Anal. Calcd. for $C_{19}H_{25}O_4N$ (331.39): C, 68.86; H, 7.60; N, 4.23. Found: C, 69.07 ; H, 7.46 ; N, 4.05.)

Methiodide. Leaflets. M. p. 274° (dec.). Easily soluble in water and alcohol.

Diacetyl derivative. Prepared by warming the base with acetic anhydride on water bath. Irregular granules from methanol. M.p. 185°. $[\alpha]_D^{18} = -95.9°$ (c 0.826, chlf.). (Anal. Calcd. for $C_{23}H_{29}O_6N$ (415.46) : C, 66.49 ; H, 7.03 ; N, 3.37. Found : C, 66.50 ; H, 7.11 ; N, 3.15.)

Methiodide of diacetyl der. Prepared in methanol. Crystallized in beautiful plates. M. p. 282°. (Anal. by titration. Calcd. for $C_{23}H_{29}O_6N \cdot JCH_3$: $2CH_3CO$, 15.44. Found : 16.28.)

Dihydrosinomeninol (III)

Sinomeninol (500 mgr.) was reduced catalytically with PtO_2 and hydrogen. The absorption of hydrogen was complete in one hour (for one double bond). The repeated recrystallization from acetone brought up the m.p. to 167°. $[\alpha]_D^{18} = +41.4°$ (c 2.101, chlf.). (Anal. Calcd. for $C_{19}H_{27}O_4N$ (333.39) : C, 68.46 ; H, 8.11 ; N, 4.21. Found : C, 68.65 ; H, 7.59 ; N. 4.03.)

For comparison, dihydrosinomenine was reduced with PtO_2 and hydrogen on its ketone group and the identical dihydrosinomeninol was obtained. M.p. 167°. Also, the mixed m.p.

β-Dihydrosinomeninone (D-6-Hydroxydihydrothebainone-7) (IV)

Sinomeninol (0.5 gr.) was heated with 20% hydrochloric acid (5 cc.) on water bath for one and half hours. The isolated base crystallized out from conc. methanol solution in hairy needles on seeding with β-dihydrosinomeninone. Yield 0.3 gr. (60%). M.p. 103°. Also, the mixed m.p. It resinified in open vessel in a week, just as β-dihydrosinomeninone from sinomeninone does (in wet climate of summer). Methiodide. Plates from methanol. M.p. 274°. Also, the mixed m.p.

Reduction of β-dihydrosinomeninone with Na-amalgam

β-Dihydrosinomeninone (2 gr.) was dissolved in 10% NaOH (10 cc.), added with 3% Na-amalgam (12 gr.) and left stand overnight. No sodium phenolate was crystallized out, and the isolated base did not make crystalline hydrobromide (difference from (+)-dihydrothebainone). M.p. 130°. Also the mixed m.p. with D-dihydrothebainone-7 was unaltered.

To assure the result, the above (+)-dihydrothebainone-7 was reduced catalytically ($PtO_2 + H_2$ in methanol) to (+)-dihydrothebainol-7, m.p. 154°, when dried at 100°. Also, the mixed m.p. with the substance prepared from tetrahydrosinomeninone[3].

β-Dihydrosinomeninone from sinomeninol (II) gave also (+)-dihydrothebainone-7, m.p. 135°, with Na-amalgam reduction.

(+)-Dihydrocodeinone (VII)

1. From β-dihydrosinomeninone. β-Dihydrosinomeninone (1 gr.) was heated with 50% sulphuric acid (8 cc.) at 120° (bath temp.) for two hours. The solution took a bluish colour after one hour's heating. The isolated base was once again purified in ether solution by repeated washing with caustic soda. Then (+)-dihydrocodeinone crystallized out in prisms on evaporation of ether. M.p. 196°. Also the mixed m.p. with the substance from other source. Yield 0.35 gr. No ferric chloride reaction.

2. From sinomeninol (II). The condition of the experiment was same as above, only 55% sulphuric acid having been employed. M.p. 193°. Yield ca. 30%.

Transformation of β-dihydrosinomeninone to α-dihydrosinomeninone. Pure β-dihydrosinomeninone (0.1 gr.) was heated with 25% sulphuric acid (10 cc.) in boiling water bath for one and half hours. From the mixture, a small quantity of α-substance was isolated. Stout prisms. M.p. 128° (sintering at 125°). The mixed m.p. was unaltered.

Crystalline Tuduranine[8]

Tuduranine was very difficultly crystallizable. But, per chance it crystallized out from ether extract in large, stout prisms. By seeding with these, it is now easy to obtain it in crystalls. M.p. 204°. $[\alpha]_D^{20} = -127.5^\circ$ (c 0.8555, ethanol). (Anal. Calcd. for $C_{18}H_{19}O_3N$ (297): C, 72.72. H, 6.40; N, 4.71. Found: C, 72.72; H, 6.54; N, 4.82.)

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References

1) 65th Comm. on Sinomenine.

2) K. Goto and K. Michi: Acta Phytochimica, **15**, 183 (1949).

3) K. Goto and K. Michi: Ibid., **15**, 187 (1949).

4) K. Goto and Y. Shibazaki: Ann., **503**, 281 (1933).

5) K. Goto, H. Shishido, and K. Takubo: Ann., **497**, 293 (1932).

6) Formerly, Epidihydrothebainone[3]. But, as the name dihydroepithebainone was already used by C. Schöpf et al. in an other substance (Ann., **452**, 211 (1927)), we think our substance should be designated with this new name.

7) K. Goto and K. Michi: Bull. Chem. Soc. Japan, **20**, 262 (1949).

8) K. Goto: Ann., **521**, 175 (1935).